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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,694	09/30/2003	Michael Brines	10165-027-999	7980

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,694	BRINES ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *1-12,15,22-30 and 33-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 14, 16-21, 31, 32, and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04/21/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/09/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV in the reply filed on 03/09/2007 is acknowledged. The traversal is on the ground(s) that Invention group VI, claim 21, should be examined together with group IV because the two invention have similar procedures and examining both groups together would not impose an undue burden o the examiner. This is found persuasive. Thus, group VI (claim 21) will be examined together with the elected group IV.
2. Claims 1-50 are pending. Claims 13, 14, 16-20 (in part), 21, 31 (in part), 32 (in part), 43-50 (in part), All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Information Disclosure Statement

3. The information disclosure statement filed on 03/09/2005 has been considered by the examiner.

Drawings

4. The drawings filed on 04/21/2004 are accepted by the Examiner.

Objection to the Disclosure

5. The disclosure is objected to because of the following informalities:

(i). it contains an embedded hyperlink (see, e.g., page 112, line 7). Applicant is required to delete the embedded hyperlink. See MPEP § 608.01.

(ii). it contains invention-unrelated text (see [0079] at page 27 and [00158] at page 62.

Appropriate correction is required.

Inventorship

6. In view of the papers filed 6/23/2005, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by addition of Thomas Coleman.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Claim Rejections—35 USC § 112, 1st paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 13, 14, 16-20, 21, 31, 32, and 43-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using a tissue protective cytokine receptor complex comprising an EPO receptor and a βc in

screening assays to identify a compound that exhibit a tissue protective activity, does not reasonably provide enablement for a method of using any other tissue protective cytokine receptor complexes in screening assays to identify a compound that exhibit a tissue protective activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 13, 14, 16-20, 21, 31, 32, and 43-50 are drawn to a method for identifying a compound that modulates a tissue activity using a tissue protective cytokine receptor complex-expressing cell. The specification states that the term "tissue protective cytokine receptor complex" may contain multiple erythropoietin receptors and/or beta common receptors, as well as other types of receptors (bottom of page 13 to top of page 14). However, the instant disclosure merely discloses a tissue protective cytokine receptor complex comprising an EPO receptor and a βc, which may be used for identifying a compound that exhibit a tissue protective activity (see Summary at page 4 and working examples). The specification does not disclose

any other types of tissue protective cytokine receptor complexes. The specification fails to provide sufficient guidance and working examples regarding on how to make and use any other types of tissue protective cytokine receptor complexes in the screening assays for identifying a compound that modulates a tissue protective activity. The prior art teaches a functional complex comprising EPO receptor (EPO-R) and a common β chain (βc) in murine Ba/F3 cells which were transfected with either murine EPO-R or EPO-R/βc (Jubinsky et al., Blood 90:1867-1873, 1997). However, there are no teachings on the use of any other types of tissue protective cytokine receptor complexes in screening for a compound that modulates a tissueprotective activity. It is unpredictable whether a given receptor forms a tissue protective cytokine receptor complex with an EPO receptor or a βc. Accordingly, it would take undue experimentation for one skilled in the art to practice the claimed method commensurate in scope with these claims.

Claim Rejections—35 USC§ 112, 2nd paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 13, 14, 16-20, 31, 32, 43-50 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 48 recites the limitation "wherein the tissue protective cytokine receptor complex ligand is an EPO". There is insufficient antecedent basis for this limitation in claims 16 or 13 from which it depends.

Claims 13, 14, 16-20, and 43-50 are indefinite because the steps recited by the methods do not necessarily achieve the goal set forth in the claim preamble. The claims recite a method comprising "contacting" and "identifying ", but fail to recite how a test compound is assayed for its tissue protective activity. It is unclear what tissue protective activity is determined.

Claim 31 is indefinite because it recites "detecting the presence of nucleolin in the cell". It is nuclear how a tissue protective activity is assayed by detecting the presence of nucleolin in the cell.

Claim 32 is rejected as dependent claim from claim 13.

Claim Rejections—35 U.S.C. §103 (a)

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 13, 14, 17, 19, 20, 48, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jubinsky et al. (Blood 90:1867-1873, 1997) in view of Mercury™ Pathway Profiling System User Manual (Clontech, March 2, 2001).

Jubinsky et al. teach a functional complex comprising EPO receptor (EPO-R) and a common β chain (βc) in murine Ba/F3 cells which were transfected with either murine EPO-R or EPO-R/βc. The Ba/F3 wild-type cells endogenously express IL-3 R 9 (and thus βc). Jubinsky et al. teach a functional role of βc in the EPO-dependent proliferation of Ba/F3 cells that express EPO-R (last paragraph of the article) and that both Ba/F3-EPO-R and Ba/F3-EPO-R+βc required EPO for survival and responded to EPO (see, e.g., bottom of right column of page 1868; Fig. 1) and a functional role of βc in the EPO-dependent proliferation of Ba/F3 cells that express EPO-R. Jubinsky et al. teach a method for identifying the effect of antisense to βc, sense, and nonsense on EPO-dependent proliferation and β globin expression in Ba/F3 cells (page 1869; Fig. 2).

Jubinsky et al. fail to teach transfection of the cells with a nucleic acid comprising a nucleotide sequence that encodes a reporter gene operably lined to a regulatory element associated with a tissue protective cytokine receptor complex activity and detect the changes in the level of reporter gene expression as recited in step (a) and (b) of claim 13

Mercury™ Pathway Profiling System User Manual teaches reporter genes--SEAP and luciferase, various vectors containing a promoter and a response element, including E2F, SRE controlling the transcription of the SEAP gene or luciferase gene (Table 1 and Fig. 2), and an assay of screening a compound for its effect based upon the reporter activity (Fig. 1).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Jubinsky et al. by inclusion of the reporter system described in the Mercury™ Pathway Profiling System User Manual with a reasonable expectation of success. One would have been motivated to do so because the reporter system described in the Mercury™ Pathway Profiling System User Manual provides an ideal reporter for signal transduction and proliferation linked to activation of a membrane receptor (see, e.g., Fig. 1 and Fig. 2).

13. Claims 13, 16-18, 21, and 43-48, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jubinsky et al. (Blood 90:1867-1873, 1997) in view of Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000).

Jubinsky et al. teach a functional complex comprising EPO receptor (EPO-R) and a common β chain (βc) in murine Ba/F3 cells which were transfected with either murine EPO-R or EPO-R/βc. The Ba/F3 wild-type cells endogenously express IL-3 R 9 (and thus βc). Jubinsky et al. teach a functional role of βc in the EPO-dependent proliferation of Ba/F3 cells that express EPO-R (last paragraph of the article) and that both Ba/F3-EPO-R and Ba/F3-EPO-R+βc required EPO for survival and responded to EPO (see, e.g., bottom of right column of page 1868; Fig. 1) and a functional role of βc in the EPO-dependent proliferation of Ba/F3 cells that express EPO-R. Jubinsky et al. teach a method for identifying the effect of antisense to βc, sense, and nonsense on EPO-dependent proliferation and β globin expression in Ba/F3 cells (page 1869; Fig. 2).

Jubinsky et al. fail to teach (i). that the tissue protective cytokine rceptor complex-expressing cell is a prokaryotic cell, a human cell, or a modified yeast cell, as recited in claims 16, 18, and 21; and (ii). that the test compound is a small molecule, a peptide, a member of library, an antibody, or a compound that binds the tissue protective cytokine receptor complex ligand, as recited in claims 43-47 and 50.

Trueheart et al. teach rapid, reliable and effective assays for screening and identifying pharmaceutically effective compounds that specifically interact with and modulate the activity of a heterologous receptor (column 2, the 3rd paragraph and last paragraph; 2nd paragraph of column 13), including cytokine receptor (see, e.g., the 3rd paragraph of column 20). Trureheart teach that the cells used in the assay can be any type of cells, whether prokaryotic or eukaryotic, including yeast cells, mammalian cells, such as HeLa cell that is a human cell (column 2, 4th paragraph; column 15, last two paragraphs). Trueheart et al. also teach the ability of particular compounds to modulate a signal transduction activity of target receptor can be detected by a reporter gene (column 13, paragraphs 2-4; column 12, lines 44-54). Trueheart et al. further teach that the test compound can be a peptide, a small organic molecule (column 11, the 3rd paragraph), and can be derived from a peptide library or a non-peptide library (column 4, the 2nd paragraph).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Jubinsky et al. to functionally express EPO-R and βc in a prokaryotic cell, such as a yeast cell, or a human cell to screen various compounds using a reporter gene taught by Trueheart

et al. to identify a compound that modulates a tissue productive activity of the EPO-R/βc complex with a reasonable expectation of success. One would have been motivated to do so because the assay system provides a rapid, reliable and effective assay for screening and identifying effectors of a receptor protein or complex thereof as taught by Trueheart et al. (the 3rd paragraph of column 2; 2nd paragraph of column 13), Moreover, it would have also been obvious to one having ordinary skill in the art at the time the invention was made to screen a test compound, which is an antibody specific for a tissue protective cytokine receptor complex or a ligand thereof, or to screen a compound that binds the tissue protective cytokine receptor complex ligand because these compounds might act as a modulator of the a tissue protective activity of a tissue protective cytokine receptor complex.

Claim Objections—Minor Informalities

14. Claims 16-20, 29-32, and 43-50 are objected to because they depend from non-elected claims. Appropriate correction is required.

Conclusion

15. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875.

The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li, Ph.D.
Primary Examiner
May 26, 2007

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